B1 on December 16, 1996. Under 35 U.S.C. §§ 119(e)(1) and 120, this application claims benefit of said applications and patent."

On page 42, in the paragraph starting on line 10, please replace with the following paragraph:

B2 The tissue was dehydrated with a graded series of ethyl alcohols, cleared with xylene, and infiltrated with PARAPLAST X-TRA (Fisher Scientific, Pittsburgh, PA) using a TISSUE-TEK VIP2000 (Miles, Inc., Elkhart, IL).

On page 42, in the paragraph starting on line 14, please replace with the following paragraph:

B3 The flattened pancreas was removed from the biopsy bag using forceps and embedded longitudinally with PARAPLAST X-TRA. All pancreata were oriented the same way in the block, with the head of the pancreas placed in one corner of the embedding mold, the tail of the pancreas in the opposite corner, and the body in the middle of the mold.

On pages 42-43, in the paragraph starting on line 25 of page 42, please replace with the following paragraph:

B4 The sections were stained with Harris hematoxylin (Sigma, St. Louis, MO) and Eosin histology staining (Surgipath, Richmond, IL). The number and size of islets per longitudinal section of the pancreas were counted and measured by using a camara-lucida attached to a light microscope (10X objective, Olympus, BH-2), interfaced to a BIOQUANT SYSTEM IV image analysis system (B&M Biometric, Inc., Nashville, TN). After calibration, the electronic pen of the digitizer was used to carefully trace the outline of each islet profile by screening the whole section of the pancreas. Simultaneously, the data was computed and stored. Data analyses were performed by using ANOVA (GraphPad Software, San Diego, CA) followed by unpaired t test.

On page 46, in the paragraph starting on line 14, please replace with the following paragraph:

B5 A sample of Zins1, purified as described above, was run on a NOVEX 18% Tris-Glycine gel (NOVEX, San Diego, CA) under reducing conditions (2-mercaptoethanol). An electroblot transfer to PVDF membrane was performed in 10mM CAPS buffer pH 11.0, 10% methanol at 200mA for 1 hour at 4°C. The PVDF blot was visualized with Coomassie

B5

blue staining. Stained protein bands were excised for Edman degradation N-terminal protein sequencing on an Applied Biosystems 476A Protein Sequencer (Foster City, CA) using standard protocols and FSTBLT cycles. The data was analyzed using Applied Biosystems Model 610A Data Analysis System, v.1.2.2).

On pages 46-47, in the paragraph starting on line 28 of page 46, please replace with the following paragraph:

B6

A Michrom BioResources MAGIC 2002 HPLC system (Michrom BioResources, Inc., Auburn, CA) equipped with a 1.0 x 150 mm Monitor C18 100Å 5m column (Michrom BioResources, Inc.) was used at a flowrate of 50 µl/min and a column temperature of 30°C. Typically, 5.0 µg of whole or digested protein was injected onto the column equilibrated in 5% B and a linear gradient from 5 to 85% B over 80 minutes was immediately initiated (A: 2% acetonitrile + 0.1% acetic acid + 0.020% TFA, B: 90% acetonitrile + 0.1% acetic acid + 0.018% TFA). The outlet from the HPLC UV detector was plumbed directly into a Finnigan LCQ Ion Trap Mass Spectrometer (Thermoquest Corp., San Jose, CA) with no flow splitting, a heated capillary temperature of 220°C, and a sheath gas flow of 75 (arbitrary units). The source voltage was 5.60 kV and the capillary voltage was 41.00 V. Mass spectra from 300-2000 m/z were recorded continuously during the gradient with 3 microscans per full scan. The most intense [M+2H]2+ ion in each spectrum was automatically selected by the LCQ for zoom scan and MSMS at 25% collision energy.

On pages 48-49, in the paragraph starting on line 24 of page 48, please replace with the following paragraph:

B7

5 µg each of untreated, PNGaseF-treated, and sialidase-treated Zins1 NF was diluted with an equal volume of NOVEX 2X Tris-Glycine SDS sample buffer (NOVEX, San Diego, CA), boiled for 3-5 minutes, and loaded onto a NOVEX 18% Tris-Glycine gel. In addition, 5 µg each of untreated, PNGaseF-treated, and sialidase-treated Zins1 NF was diluted with an equal volume of NOVEX 2X Tris-Glycine SDS sample buffer (NOVEX, San Diego, CA) containing 5% b-mercaptoethanol, boiled for 3-5 minutes, and loaded onto a NOVEX 18% Tris-Glycine gel. Both the non-reduced and reduced gels were run at a constant voltage of 125V and visualized with Coomassie Blue staining. NOVEX Mark 12 Wide Range Protein Standards were used to determine apparent molecular weights.

On page 49, in the paragraph starting on line 17, please replace with the following paragraph:

B8

Confirmation of the putative O-glycosylation was obtained via monosaccharide composition analysis. Monosaccharide composition for Zins1 was analyzed as follows: Monosaccharide composition was carried out on a Dionex system composed of a DX500 HPLC with an ED40 electrochemical detector, a GP40 pump, and a CARBOPAC-PA 10 column (Dionex, Sunnydale, CA). In both types of analyses, Dionex monosaccharide standards were used to calibrate the instrument. The glycoprotein fetuin was used as a positive control (Sigma, St. Louis, MO).

On page 55, in the paragraph starting on line 1, please replace with the following paragraph:

B9

Conditioned culture medium removed from these islet cells was added to cultures of normal BALB/c islets were isolated in MATRIGEL Basement Membrane Matrix (Collaborative Biomedical Products, Bedford, MA). The normal mouse islet phenotype changed, becoming huge with much branching and forming cyst-like structures. This conditioned medium was designated IDC53.1. Various other conditioned media obtained either from cultures of osteoclast, osteoblast or dendritic cells obtained from p53-/- knockout mice (see WO 9607733), or from cultures of normal C57/Black 6 islet cells, did not exhibit this activity. In addition, normal BALB/c islets placed in this conditioned medium developed "cobblestone" cells all around the islet. This effect was not seen when various other conditioned media were tested.

On pages 56-57, in the paragraph starting on line 29 of page 56, please replace with the following paragraph:

B10

The islet preparation was then mounted on glass slides with depressions to prevent the islets from losing their shape. FLUOROGUARD Antifade Reagent (BioRad, Hercules, CA) was the mounting medium used. All positive BrdU cells per islet were counted for each of the three harvest days. On Day 4, there were 1.5 times more positive cells in the islets cultured in the 5X IDC53.1 CM than in the control. On Day 8, there were 2.9 times more positive cells, and on Day 12 there were 3.5 times more positive cells, as compared to the control.

On page 63, please delete the title and insert the rewritten title:

B11 "ZINS1 POLYPEPTIDE COMPOSITION STIMULATING PANCREATIC ISLET GROWTH".

In the Claims:

Please amend claim 1 as follows:

B12 1. An isolated protein produced by a method comprising:

culturing a host cell into which has been introduced a DNA expression vector comprising the following operably linked elements:

a transcription promoter;

a DNA segment comprising a nucleotide sequence shown in SEQ ID NO: 1 from nucleotide 76 to nucleotide 417; and

a transcription terminator, wherein said host cell expresses the polypeptide encoded by said DNA segment; and

recovering said protein.

Please cancel claims 4 and 5.

REMARKS

Claim 1 has been amended. Claims 2 and 3 incorporate the amendment by virtue of their dependency. Claims 4 and 5 have been canceled. Claims 1-3 are pending.

The specification has been objected to for certain informalities. These informalities have been corrected by amendment to the specification. The errors were typographical and inadvertent. No new matter is introduced by these amendments. The title of the instant patent application has been amended to conform with the Examiner's recommendation. This amendment does not change the scope of the claimed inventions because it does not relate to patentability but to formalities. These amendments obviate the Examiner's objections, and Applicants respectfully request the objections be withdrawn.

Claims 4 and 5 have been objected to for certain informalities. These claims have been canceled, and therefore the objections have been obviated. Applicants request the objections be withdrawn.